

what is claimed is:

1. A method of assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising:

(a) collecting a plasma sample from the HIV-infected patient; and

(b) evaluating whether the plasma sample contains nucleic acid encoding HIV reverse transcriptase having a mutation at codon 236;

in which the presence of the mutation correlates with decreased susceptibility to delavirdine and little or no change in nevirapine susceptibility.

2. The method of claim 1, wherein the mutation at codon 236 codes for a leucine.

3. The method of claim 1, wherein reverse transcriptase has an additional mutation(s) at codon 103, codon 181 or a combination thereof.

4. The method of claim 3, wherein the mutation at codon 103 encodes an asparagine (N) and the mutation at codon 181 encodes a cysteine (C).

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5. The method of claim 1, wherein the HIV-infected patient is being treated with an antiretroviral agent.

6. A method of assessing the effectiveness of antiretroviral therapy of an HIV-infected patient comprising:

(a) collecting a biological sample from an HIV-infected patient; and

(b) evaluating whether the biological sample comprises nucleic acid encoding HIV reverse transcriptase having a mutation at codon 225;

in which the presence of the mutation correlates with an increase in delavirdine susceptibility and little or no change in nevirapine susceptibility.

7. The method of claim 6 wherein the mutated codon 225 encodes a histidine (H).

8. The method of claim 6, wherein the HIV-infected patient is being treated with an antiretroviral agent.

9. The method of claim 6, wherein the reverse transcriptase has an additional mutation(s) at codon 103, 181 or a combination thereof.

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- in which the presence of the mutation correlates with an increase in delavirdine susceptibility and a decrease in nevirapine susceptibility.

11. The method of claim 10, wherein the mutation at codon 190 encodes an alanine or a serine.

12. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

- (a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation at codon 236 and a mutation at codon 103 and/or 181 and an indicator gene into a host cell;
- (b) culturing the host cell from step (a);
- (c) measuring the indicator in a target host cell; and
- (d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the

absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

13. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

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- (a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation at codon 225 and a mutation at codon 103 and an indicator into a host cell;
  - (b) culturing the host cell from step (a);
  - (c) measuring the indicator in a target host cell; and
  - (d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

14. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

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(c) measuring expression of the indicator gene in a target host cell; and

wherein a test concentration of the candidate anti-viral drug compound is present at steps (a)-(c); at steps (b)-(c); or at step (c).

(a) introducing a resistance test vector comprising a patient-derived segment which encodes the reverse transcriptase having a mutation at codon 225, and an indicator gene into a host cell;

(c) measuring expression of the indicator gene in a target host cell; and

(d) comparing the expression of the indicator gene from step (c) with the expression of the indicator gene measured when steps (a)-(c) are carried out in the absence of the candidate anti-viral drug compound,

wherein a test concentration of the candidate anti-viral drug compound is present at steps (a)-(c); at steps (b)-(c); or at step (c).

16. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

(a) introducing a resistance test vector comprising a patient-derived segment further comprising reverse transcriptase having a mutation at codon 190, and an indicator gene into a host cell;

(b) culturing the host cell from step (a);

(c) measuring expression of the indicator gene in a target host cell; and

(d) comparing the expression of the indicator gene from step (c) with the expression of the indicator gene measured when steps (a)-(c) are carried out in the absence of the candidate anti-viral drug compound;

wherein a test concentration of the candidate anti-viral drug compound is present at steps (a)-(c); at steps (b)-(c); or at step (c).

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17. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutation at codon 190 and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

18. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutation at codon 225 and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

19. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutation at codon 236 and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

20. The resistance test vector of claim 17, wherein the patient-derived segment having a mutation at codon 190 further comprises a mutation at codon 103.

21. The resistance test vector of claim 18, wherein the patient-derived segment having a mutation at codon 225 further comprises a mutation at codon 103.

22. The resistance test vector of claim 17, wherein the patient-derived segment having a mutation at codon 236 further comprises a mutation at codon 103 and/or 181.

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(b) evaluating whether the plasma sample contains nucleic acid encoding HIV reverse transcriptase having a mutation at codon 230;

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27. The method of claim 23, wherein the HIV-infected patient is being treated with an antiretroviral agent.

28. A method of assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising:

(a) collecting a plasma sample from the HIV-infected patient; and

(b) evaluating whether the plasma sample contains nucleic acid encoding HIV reverse transcriptase having a mutation at codon 181;

in which the presence of the mutation correlates with decreased susceptibility to delavirdine and nevirapine and little or no change in efavirenz susceptibility.

29. The method of claim 28, wherein the mutation at codon 181 codes for a cysteine (C).

30. The method of claim 28, wherein reverse transcriptase has an additional mutation(s) at codon 98, codon 106, codon 227 or a combination thereof.

31. The method of claim 30, wherein the mutation at codon 98 encodes a glycine (G), the mutation at codon 106 encodes an alanine (A) and the mutation at codon 227 encodes a leucine (L).

32. The method of claim 28, wherein the HIV-infected patient is being treated with an antiretroviral agent.

33. A method of assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising:

(a) collecting a plasma sample from the HIV-infected patient; and

(b) evaluating whether the plasma sample contains nucleic acid encoding HIV reverse transcriptase having a mutation at codon 188,

in which the presence of the mutation correlates with decreased susceptibility to delavirdine and nevirapine and efavirenz.

34. The method of claim 33, wherein the mutation at codon 188 codes for a leucine (L), cysteine (C) or histidine (H).

35. The method of claim 33, wherein reverse transcriptase has an additional mutation(s) at codon 138, codon 103, codon 100 or a combination thereof.

36. The method of claim 35, wherein the mutation at codon 138 encodes an alanine (A), the mutation at codon 103 encodes an asparagine (N) and the mutation at codon 100 encodes an isoleucine (I).

37. The method of claim 33, wherein the HIV-infected patient is being treated with an antiretroviral agent.

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38. A method of assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising:

(a) collecting a plasma sample from the HIV-infected patient; and

(b) evaluating whether the plasma sample contains nucleic acid encoding HIV reverse transcriptase having a mutation at codon 190;

in which the presence of the mutation correlates with increased susceptibility to delavirdine and decreased susceptibility to nevirapine and efavirenz.

39. The method of claim 38, wherein the mutation at codon 190 codes for an alanine (A) or a serine (S).

40. The method of claim 38, wherein reverse transcriptase has an additional mutation(s) at codon 98, codon 101 or codon 103 or a combination thereof.

41. The method of claim 40, wherein the mutation at codon 98 encodes a glycine (G), 101 encodes a glutamic acid (E) and 103 encodes an asparagine (N).

42. The method of claim 38, wherein the HIV-infected patient is being treated with an antiretroviral agent.

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(b) evaluating whether the plasma sample contains nucleic acid encoding HIV reverse transcriptase having a mutation at codon 106;

44. The method of claim 43, wherein the mutation at codon 106 encodes an alanine (A).

45. The method of claim 43, wherein reverse transcriptase has an additional mutation(s) at codon 227 and codon 189 or a combination thereof.

46. The method of claim 45, wherein the mutation at codon 227 encodes a leucine (L) and 189 encodes a leucine (L).

47. The method of claim 43, wherein the HIV-infected patient is being treated with an antiretroviral agent.

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(b) evaluating whether the plasma sample contains nucleic acid encoding HIV reverse transcriptase having a mutation at codon 103;

49. The method of claim 48, wherein the mutation at codon 103 codes for asparagine (N).

50. The method of claim 48, wherein reverse transcriptase has an additional mutation(s) at codon 100 or a combination thereof.

51. The method of claim 50, wherein the mutation at codon 100 encodes an isoleucine (I).

52. The method of claim 48, wherein the HIV-infected patient is being treated with an antiretroviral agent.

53. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

(a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation at codon 230 and a mutation at codon 181 and an indicator gene into a host cell;

(b) culturing the host cell from step (a);

(c) measuring the indicator in a target host cell; and

(d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

54. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

(a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation at codon 181 and a mutation at codon 98 and/or 106 and/or 227 and an indicator gene into a host cell;

(b) culturing the host cell from step (a);

(c) measuring the indicator in a target host cell; and

(d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the

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absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

55. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

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- (a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation at codon 188 and a mutation at codon 138 and/or 103 and/or 100 and an indicator gene into a host cell;
  - (b) culturing the host cell from step (a);
  - (c) measuring the indicator in a target host cell; and
  - (d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

56. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

- (a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation



at codon 190 and a mutation at codon 98 and/or 101 and/or 103 and an indicator gene into a host cell;

(b) culturing the host cell from step (a);

(c) measuring the indicator in a target host cell; and

(d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

57. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

- (a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation at codon 106 and a mutation at codon 227 and/or 189 and an indicator gene into a host cell;
- (b) culturing the host cell from step (a);
- (c) measuring the indicator in a target host cell; and
- (d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

58. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

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- (a) introducing a resistance test vector comprising a patient-derived segment further comprising a mutation at codon 103 and a mutation at codon 100 and an indicator gene into a host cell;
  - (b) culturing the host cell from step (a);
  - (c) measuring the indicator in a target host cell; and
  - (d) comparing the measurement of the indicator from step (c) with the measurement of the indicator measured when steps (a) - (c) are carried out in the absence of the candidate antiretroviral drug compound;

wherein a test concentration of the candidate antiretroviral drug compound is present at steps (a) - (c); at steps (b) - (c); or at step (c).

59. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

- (a) introducing a resistance test vector comprising a patient-derived segment which encodes the reverse transcriptase having a mutation at codon 230 and an indicator gene into a host cell;

(b) culturing the host cell from step (a);

(c) measuring expression of the indicator gene in a target host cell; and

(d) comparing the expression of the indicator gene from step (c) with the expression of the indicator gene measured when steps (a)-(c) are carried out in the absence of the candidate anti-viral drug compound,

wherein a test concentration of the candidate anti-viral drug compound is present at steps (a)-(c); at steps (b)-(c); or at step (c).

60. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

(a) introducing a resistance test vector comprising a patient-derived segment which encodes the reverse transcriptase having a mutation at codon 227 and an indicator gene into a host cell;

(b) culturing the host cell from step (a);

(c) measuring expression of the indicator gene in a target host cell; and

(d) comparing the expression of the indicator gene from step (c) with the expression of the indicator gene measured when steps (a)-(c) are carried out in the absence of the candidate anti-viral drug compound,

wherein a test concentration of the candidate anti-viral drug compound is present at steps (a)-(c); at steps (b)-(c); or at step (c).

61. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

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- (a) introducing a resistance test vector comprising a patient-derived segment which encodes the reverse transcriptase having a mutation at codon 188 and an indicator gene into a host cell;
  - (b) culturing the host cell from step (a);
  - (c) measuring expression of the indicator gene in a target host cell; and
  - (d) comparing the expression of the indicator gene from step (c) with the expression of the indicator gene measured when steps (a)-(c) are carried out in the absence of the candidate anti-viral drug compound,

wherein a test concentration of the candidate anti-viral drug compound is present at steps (a)-(c); at steps (b)-(c); or at step (c).

62. A method for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising:

- (a) introducing a resistance test vector comprising a patient-derived segment which encodes the reverse

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- wherein a test concentration of the candidate anti-viral drug compound is present at steps (a)-(c); at steps (b)-(c); or at step (c).

63. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutation at codon 230 and an indicator gene, wherein the expression of the indicator gene is dependant upon the patient derived segment.

64. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutation at codon 227 and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

65. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutation at codon 188 and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

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66. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutation at codon 189 and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

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67. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutations at codon 181, codon 98, codon 106 and codon 227 or a combination thereof and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

68. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutations at codon 106, codon 227, and codon 189 or a combination thereof and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

69. A resistance test vector comprising an HIV patient-derived segment further comprising reverse transcriptase having a mutations at codon 103 and codon 101 and an indicator gene, wherein the expression of the indicator gene is dependent upon the patient derived segment.

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70. The resistance test vector of claim 17, wherein the patient-derived segment having a mutation at codon 190 further comprises mutations at codon 98 and codon 101 or a combination thereof.

71. The resistance test vector of claim 63, wherein the patient-derived segment having a mutation at codon 230 further comprises a mutation at codon 181.

72. The resistance test vector of claim 65, wherein the patient-derived segment having a mutation at codon 188 further comprises mutations at codon 138, codon 103 and codon 190 or a combination thereof.

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